

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A method for the treatment of a disease or disorder by modulating the activity of at least one neurotrophin and/or a pro-neurotrophin in an organism in need thereof, said method comprising administering to said organism individual Use of an effective amount of an agent
capable of

(i) binding to a receptor of the Vps10p-domain receptor family and/or

(ii) interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin

and/or

(iii) modulating the expression of a receptor of the Vps10p-domain receptor family;

~~in the manufacture of a medicament for use in a method for treatment of a disease or disorder by modulating the activity~~

~~of at least one neurotrophin and/or a pro-neurotrophin in an organism, such as an animal.~~

2. (currently amended) The ~~use~~ method according to claim 1, wherein said method ~~medicament~~ is for the treatment of a neurological disease or disorder, ~~such as a neural disorder.~~

3. (currently amended) The ~~use~~ method according to claim 1, ~~any of the preceding claims,~~ wherein the modulation is a decrease of the activity.

4. (currently amended) The ~~use~~ method according to ~~any of claims 1-2,~~ wherein the modulation is an increase of the activity.

5. (currently amended) The ~~use~~ method according to ~~any of the preceding claims~~ claim 1, wherein the neurotrophin is selected from the group consisting of: neural growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and neurotrophin-4/5 (NT-4/5).

6. (cancelled)

7. (currently amended) The ~~use~~ method according to claim 1, ~~any of the claims 1-4~~, wherein the pro-neurotrophin is selected from the group consisting of: pro-NGF, pro-BDNF, pro-NT-3 or pro-NT-4/5.

8-9. (cancelled)

10. (currently amended) The ~~use~~ method according to ~~claim 9~~1, wherein the ~~mammal~~ organism is a human being.

11. (currently amended) The ~~use~~ method according to ~~any of the preceding claims~~ claim 1, wherein the receptor is selected from the group consisting of: SorLA, Sortilin, SorCS1, SorCS-2, ~~or~~ and SorCS-3.

12. (cancelled)

13. (currently amended) The ~~use~~ method according to claim 1, ~~any of the preceding claims~~, wherein the agent is selected from the group consisting of: proteins, peptides, polypeptides, antibodies, antisense RNA, antisense-DNA or organic molecules, and SiRNA.

14. (currently amended) The ~~use~~ method according to claim 1, ~~any of the preceding claims~~, wherein the agent is capable of inhibiting binding of said neurotrophin or said pro-neurotrophin to the receptor.

15. (currently amended) The ~~use~~ method according to claim 1, ~~any of the preceding claims~~, wherein the agent is capable of binding to an extracellular part of the receptor.

16. (currently amended) The ~~use~~ method according to claim 1, ~~any of the preceding claims~~, wherein the agent is an antibody directed against, an extracellular part of the receptor, an intracellular part of the receptor, or a transmembrane part of the receptor.

17. (currently amended) The ~~use~~ method according to claim 16, wherein the agent is an antibody directed against a peptide comprising a sequence ~~having comprising~~ SEQ ID NO: 1 amino acid residues 612-740 of SEQ ID NO:1.

18. (currently amended) The ~~use~~ method according to claim 15, ~~any of the claims 1-15~~, wherein the agent is a peptide comprising a sequence ~~having comprising~~ SEQ ID NO: 1

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amino acids 24-77 of SEQ ID NO:1, or a variant thereof, said peptide being capable of binding to the receptor.

19. (currently amended) The ~~use~~ method according to claim 18, wherein the variant comprises or consists of ~~is~~ ~~selected from one or more of the following sequences: SEQ ID NO: 2~~ amino acid residues 29-81 (propart from SorLa) of SEQ ID NO:2.

20. (currently amended) The ~~use~~ method according to claim 18, wherein the peptide is capable of binding to the receptor and comprises one or more of the ~~following~~ sequences in the group consisting of: SEQ ID NO: 6, amino acid residues 19-121 (propart for NGF) [[,]]; SEQ ID NO 7, amino acid residues 19-127 (propart for BDNF) [[,]]; SEQ ID NO: 8, amino acid residues 17-124 (propart for neurotrophin-3 (NT-3) [[,]]; SEQ ID NO: 9, amino acid residues 25-80 (propart for neurotrophin-4 (NT-4)); and ~~or a fragments~~ or a variants thereof, ~~said peptide being capable of binding to the receptor..~~

21. (currently amended) The ~~use~~ method according to claim 1, ~~or 20~~, wherein the agent is a peptide comprising a Sortilin receptor-binding sequence of proNGF.

22. (currently amended) The ~~use~~ method according to claim 20, wherein the agent is a peptide capable of binding to the receptor that comprises ~~comprising~~ the sequence SEQ ID NO: 6, amino acid residues 19-121 (the sequence from the pro-part of NGF) or a variant thereof, ~~said peptide being capable of binding to the receptor.~~

23. (currently amended) The ~~use~~ method according to claim 21, wherein the agent is a peptide consisting of the following sequence: SEQ ID NO: 6, amino acid residues 19-121 (propeptide of proNGF).

24. (currently amended) The ~~use~~ method according to claim 1, any of the claims 1-15, wherein the agent is a peptide capable of binding to the receptor that comprises ~~having~~ the sequence of SEQ ID NO: 10 or SEQ ID NO: 11, or a fragment or a variant thereof, ~~said peptide being capable of binding the receptor.~~

25. (currently amended) The ~~use~~ method according to claim 1, any of the claims 1-15, wherein the agent is a peptide comprising an NGF variant or a Sortilin-receptor binding fragment of said NGF variant.

26. (cancelled)

27. (currently amended) The ~~use~~ method according to claim 1, ~~any of claims 1-13~~, wherein the ~~variant agent~~ is ~~selected from one or more of the following sequences:~~ SEQ ID NO: 2 amino acid residues 47-66.

28. (currently amended) The ~~use~~ method according to ~~any of claims 1-13~~ claim 1, wherein the ~~variant agent~~ is ~~selected from one or more of the following sequences:~~ SEQ ID NO: 13

29. (currently amended) The ~~use~~ method according to ~~any of the claims 1-13~~ claim 1, wherein the agent is a fragment or variant of RAP (receptor-associated protein - SEQ ID NO. 12).

30. (currently amended) The ~~use~~ method according to claim 29, wherein said agent is from 20 to 60 amino acids long and ~~contains~~ comprises the preferred domain amino acid positions 219-323 of receptor-associated protein.

31. (currently amended) The ~~use~~ method according to claim 1, any of the claims 1-13, wherein the agent is a peptide comprising a sequence ~~having~~ comprising amino acids 34-77 of SEQ ID NO: 1 amino acids 34-77, or a variant thereof, said peptide being capable of binding to the receptor.

32. (currently amended) The ~~use~~ method according to claim 1, any of the claims 1-13, wherein the agent is a peptide comprising a sequence comprising amino acids 50-70 of ~~having~~ SEQ ID NO: 1 ~~amino acids 50-70~~ or a variant thereof, said peptide being capable of binding to the receptor.

33. (currently amended) The ~~use~~ method according to claim 1, wherein the disease or disorder is selected from the group consisting of: one or more of the following diseases or disorders: inflammatory pain, diseases or disorders of pancreas, kidney disorders, lung disorders, cardiovascular disorders, various types of tumours, psychiatric disorders ~~or~~ and neuronal disorders.

34. (currently amended) The ~~use~~ method according to claim 1, wherein the disease or disorder is selected from the group consisting of: Alzheimer's disease, Parkinson's disease, Huntington's chorea, stroke, ALS, peripheral

neuropathies, necrosis or loss of neurons, nerve damage to trauma, kidney dysfunction, injury, and the toxic effects of chemotherapeutics used to treat cancer and AIDS, aberrant sprouting in epilepsy, schizophrenia, pancreas or lung injury and/or dysfunction, and injury and/or dysfunction of the central and/or peripheral nervous systems.

35. (currently amended) The ~~use~~ method according to claim 1, wherein the disease or disorder is selected from the group consisting of: peripheral neuropathy, distal sensorimotor neuropathy, or autonomic neuropathies, such as reduced motility of the gastrointestinal tract or atony of the urinary bladder, post-polio syndrome or AIDS-associated neuropathy; hereditary neuropathies, such as Charcot-Marie-Tooth disease, Refsum's disease, Abetalipoproteinemia, Tangier disease, Krabbe's disease, Metachromatic leukodystrophy, Fabry's disease, and Dejerine-Sottas syndrome, depression, mania ~~or~~ and Down's syndrome.

36. (currently amended) The ~~use~~ method according to claim 1, wherein said ~~medicament~~ agent is for the development, ~~maintenance~~ maintenance, or regeneration of neurons in an individual.

37. (currently amended) The ~~use~~ method according to claim 1, wherein said ~~medicament-agent~~ is for the treatment of nerves damage by any cause in the group consisting of: eoused ~~by any of the following:~~ trauma, bums, kidney dysfunction or injury, pancreatic dysfunction or injury, lung dysfunction or injury, injury to fatty tissue, ~~or~~ and the toxic effects of chemotherapeutics used to treat cancer and AIDS.

38-39. (cancelled)

40. (currently amended) The ~~use~~ method according to claim 1, wherein said ~~medicament is for the treatment~~ is for ~~of human neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's Syndrome, nerve deafness, and Meniere's disease.~~

41. (currently amended) The ~~use~~ method according to claim 1, wherein said ~~medicament is for the treatment~~ is for ~~of a motoneuron disorders, such as amyotrophic lateral sclerosis (Lou Gehrig's disease), Bell's palsy, and various conditions involving spinal muscular atrophy, or paralysis.~~

42. (currently amended) The ~~use~~ method according to claim 1, wherein the disease or disorder is a neuropathy, ~~such as peripheral neuropathy.~~

43. (currently amended) The ~~use~~ method according to claim 1, wherein the disease or disorder is depression or mania.

44. (currently amended) The ~~use~~ method according to claim 1, wherein said ~~medicament~~ agent is ~~to be~~ used as a cognitive enhancer, ~~such as to enhance learning in individuals suffering from dementia or trauma.~~

45. (currently amended) The ~~use~~ method according to ~~any of the preceding claims~~ claim 1, wherein the agent is administered in an amount of from 1 µg/kg to about 100 mg/kg per day.

46. (currently amended) An in vitro method for screening for a compound which alters the binding of at least one neurotrophin and/or a pro-neurotrophin to a receptor of the Vps10p-domain receptor family, which comprises

- a) providing an assay for measuring the binding of a neurotrophin and/or a pro-neurotrophin to a receptor of the Vps10p-domain receptor family,
- b) adding the compound to be tested to the assay, and
- c) determining the amount of a neurotrophin and/or a pro-neurotrophin bound to the receptor of the Vps10p-domain receptor family, and
- d) comparing the amount determined in step c) with an amount measured in the absence of the compound to be tested,
- e) wherein a difference in the two amounts identifies a compound which alters the binding of neurotrophins and/or pro-neurotrophins to the receptor of the Vps10p-domain receptor family.

47. (currently amended) The method according to claim 46, wherein the neurotrophin or pro-neurotrophin is ~~as described in any of claims 5-8.~~ selected from the group consisting of: neural growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and neurotrophin-4/5 (NT-4/5).

48. (currently amended) The method according to claim 46, any one of claims 46-47, wherein the receptor is as described in any of claims 11-12. selected from the group consisting of: SorLA, Sortilin, SorCS1, SorCS-2, and SorCS-3.

49. (currently amended) The method according to claim 46, any one of claims 46-48, wherein the neurotrophin and/or pro-neurotrophin is capable of binding to an extracellular part of the receptor, an intracellular part of the receptor or a transmembrane part of the receptor.

50. (currently amended) The method according to claim 46, any one of claims 46-49, wherein the receptor is expressed in a cell and/or presented on a cell plasma membrane.

51. (currently amended) The method according to claim 50, wherein the cell is selected from the group consisting of: peripheral neurons, central neurons, primary cultures of neuronal cells, neuron-derived cell-lines and transfected cells capable of expressing and/or presenting a receptor of the Vps10p-domain receptor family.

52. (currently amended) A method for determining the effect of an agent on activity of neurotrophins and/or pro-neurotrophins in cells expressing a receptor of the Vps10p-domain receptor family, said method comprising the steps of

a) administering said agent to a mammal naturally expressing the receptor,

b) measuring the activity of neurotrophins and/or pro-neurotrophins in said mammal,

c) comparing the measurement of step b) with a measurement obtained in the absence of the compound to be tested,

d) wherein the difference in the two measurements identifies the effect of said agent on the activity of neurotrophins on cells presenting receptors of the Vps10p-domain receptor family.

53-54. (cancelled)

55. (currently amended) A method for modulating the transport of at least one neurotrophin and/or pro-neurotrophin

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out of, into or within a cell line expressing a receptor of the Vps10p-domain receptor family,

comprising administering a sufficient amount of an agent capable of binding a receptor of the Vps10p-domain receptor family in order to modulate such transport.

56-59. (cancelled)

60. (currently amended) The method according to claim 55, any one of claims 55-59, wherein the agent is as defined in any of the claims 1-32. capable of

(i) binding to a receptor of the Vps10p-domain receptor family and/or

(ii) interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin

and/or

(iii)modulating the expression of a receptor of the Vps10p-domain receptor family.

61. (currently amended) ~~Use of an agent capable of binding a receptor of the Vps10p-domain receptor family in the manufacture of a medicament for use in a~~ A method for

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treatment of an animal by modulating the transport of at least one neurotrophin and/or pro-neurotrophin out of, into or within a cell expressing a receptor of the Vps10p-domain receptor family in said animal, said method comprising administering to said animal a sufficient amount of ~~said agent~~ an agent capable of binding a receptor of the Vps10p-domain receptor family to modulate such transport.

62. (currently amended) The ~~use~~ method according to claim 61, wherein said agent is ~~as defined in any of claims 1-32.~~ capable of

(i) binding to a receptor of the Vps10p-domain receptor family and/or

(ii) interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin

and/or

(iii)modulating the expression of a receptor of the Vps10p-domain receptor family.

63. (cancelled)

64. (currently amended) A method of isolating a compound capable of altering the binding of at least one

neurotrophin and/or proneurotrophin to a receptor of the Vps10p-domain receptor family, comprising the steps of

a) screening a compound as defined in claim 46 ~~any of claims 46-60~~

b) selecting a compound altering the binding of at least one neurotrophin and/or pro-neurotrophin to a receptor of the Vps10p-domain receptor family,

c) isolating the compound of step b).

65. (cancelled)

66. (currently amended) A method of producing a pharmaceutical composition comprising the steps of claims 64 ~~or 65~~ and further the step of formulating the ~~refined~~ compound/~~compound with reduced toxicity~~ with a pharmaceutically acceptable carrier or diluent.

67-69. (cancelled)

70. (currently amended) A pharmaceutical composition comprising ~~an agent as defined in any of claims 17-32~~ an antibody directed against a peptide comprising a sequence

comprising amino acids 612-740 of SEQ ID NO:1, and a
pharmaceutically acceptable carrier.

71.(currently amended) A ~~The~~ pharmaceutical
composition comprising according to claim 70, wherein said
~~agent is~~ a soluble receptor of the Vps10p-domain receptor
family, or a fragment or a variant thereof.